REMARKS

Amendments

Claim 1 is amended to expressly recite administration to the host and to use language in accordance with conventional practice. Claim 1 is also amended to expressly recite substituent groups mentioned within the specification. See, e.g., page 27, line 25-page 28, line 17 and page 13, lines 3-10. In addition, claim 1 is amended to recite that D_1 and D_2 are not both H. See, e.g., page 13, lines 3-26 and *In re Johnson,* 194 USPQ 187 (CCPA 1977).

Claims 2 and 15 are amended to depend from new claim 19 which recites that the method is one of treatment. The remaining claims are amended to use language in accordance with US conventional practice. Claims 12-13 and 15-18 are amended to delete parenthetical expressions. Also, claim 14 is amended to delete superfluous language.

New claims 19-41 are directed to further aspects of applicants' invention. See, e.g., for example, the original claims, page 8, line 29-page 10, line 17, page 10, line 29-page 12, line 15, page 12, line 22-page 13, line 8, page 27, line 25-page 28, line 17, page 29, lines 1-3, page 32, line 32-page 33, line 3, page 33, lines 10-13, and page 38, line 32-page 39, line 8.

Claim Objections

Claim 1 is amended to expressly recite administration to the host and to correct grammatical errors. Withdrawal of the objection is respectfully requested.

Rejection Under 35 USC §112, second paragraph

Contrary to the assertion in the rejection, the term "analogue" in the contest of nucleoside bases is not indefinite. Further, applicants describe in their specification the types of structures included within this. See, e.g., the various listings of bases for group B. See also the discussion of "analogue" at page 27, lines 7-23. One of ordinary skill in this art can readily recognize whether a compound exhibits a purine or pyrimidine analogue structure. See, for example, Chemistry of Nucelosides and Nucleotides, Vols. 1 and 2, (Edited by Leroy B. Townsend, 1988).

The term "carbonyl substituted by..." is sufficiently definite. One of ordinary skill in the art would understand that it is the carbon atom of the carbonyl which is substituted. The oxygen

atom, which is attached to the carbon atom by a double bond, can not be substituted.

Applicants disagree that, in the context of the claims, 'can also be" is indefinite. In any event, claim 1 is amended to delete this phrase. In addition, claims 12 and 13 are amend to delete the superfluous parenthetical expression and claim 14 is also amended to delete superfluous language.

Withdrawal of the rejection is respectfully requested.

Rejection Under 35 USC §102(e)

Claims 1, 2, 4, 6, 10, 12, 15, and 16 are rejected as allegedly being anticipated in view of Tan et al. (WO 00/50064). Applicants respectfully traverse.

Tan et al. does not constitute prior art under 35 USC §102 (e). While Tan et al. is an international patent application published in English, the application was filed February 25, 2000, i.e., prior to November 29, 2000. Thus, WO 00/50064 is not prior art under 35 USC §102 (e). Furthermore, its publication date of August 31, 2000 is subsequent to applicants' priority date under 35 USC §119, i.e., the provisional application filing date.

Further, the rejection refers to the compounds recited in Table 1 of WO 00/50064. In those compounds where X is -O-, R^1, R^2 and R^3 are all OH. These compounds do not anticipate applicants claim 1. In addition, WO 00/50064 provides no motivation to modify the compounds described therein in such a manner so as to arrive at a compound as recited in applicants' claim 1. Withdrawal of the rejection is respectfully requested.

Rejection Under 35 USC §103

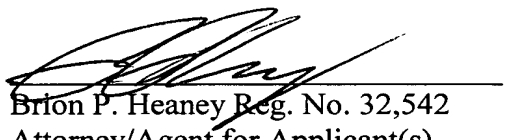
Claims 1-18 are rejected as allegedly being obvious in view of Tan et al. (WO 00/50064) taken in combination with Johansson et al. (US '215) and Hamedi-Sangsari et al. (US '522). Applicants respectfully traverse.

As discussed above, Tan et al. does not constitute prior art. Nor does Tan et al. suggest the compounds recited in applicant's claim 1. Johansson et al. (US '215) and Hamedi-Sangsari et al. (US '522) do not overcome the deficiencies of Tan et al. Withdrawal of the rejection is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version With Markings To Show Changes Made"**.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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Attorney Docket No.: PHARMA-115

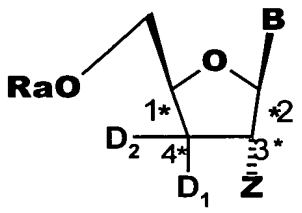
Date: April 23, 2003

Version With Markings To Show Changes Made

IN THE CLAIMS

Please amend the claims as follows:

--1. A method for the treatment or prevention of an hepatitis C infection in a host comprising administering to said host a therapeutically effective amount of a compound having the formula Ib or a pharmaceutically acceptable salt thereof:

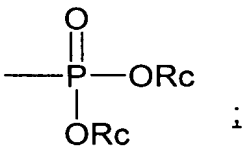


(Ib)

wherein

B is ~~chosen from~~ a purine, a pyrimidine or an analogue thereof;

Ra is ~~chosen from~~ H, monophosphate, diphosphate, triphosphate, carbonyl substituted by ~~with~~ a straight chain, branched chain or cyclic C_{1-6} alkyl which is unsubstituted or substituted by or substituted by halogen, nitro, $CONH_2$, COOH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, O-C_{2-6} alkynyl, hydroxyl, amino, or COOQ, C_{2-6} alkenyl which is unsubstituted or substituted by or substituted by halogen, nitro, $CONH_2$, COOH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, O-C_{2-6} alkynyl, hydroxyl, amino, or COOQ, C_{2-6} alkynyl which is unsubstituted or substituted by or substituted by halogen, nitro, $CONH_2$, COOH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, O-C_{2-6} alkynyl, hydroxyl, amino, or COOQ, or C_{6-10} aryl which is unsubstituted or mono- or di-substituted with OH, SH, amino, halogen or C_{1-6} alkyl, ~~and~~ or



~~wherein~~

~~each~~ Rc is, in each case ~~are~~ independently, ~~chosen from~~ H, straight chain, branched chain or cyclic C_{1-6} alkyl which is unsubstituted or substituted by or substituted by halogen, nitro, $CONH_2$, COOH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, O-C_{2-6} alkynyl, hydroxyl, amino, or COOQ, C_{2-6} alkenyl which is unsubstituted or substituted by or substituted by halogen, nitro, $CONH_2$, COOH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, O-C_{2-6} alkynyl, hydroxyl, amino, or COOQ, C_{2-6} alkynyl which is unsubstituted or substituted by or substituted by halogen, nitro, $CONH_2$, COOH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, O-C_{2-6} alkynyl, hydroxyl, amino, or COOQ, C_{6-10} aryl which is unsubstituted or mono- or di-substituted with OH, SH, amino, halogen or C_{1-6} alkyl, or a ~~and an~~ hydroxy protecting group; ~~and~~

Q is C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl;

Z is ORb;~~, wherein~~

Rb is ~~chosen from of~~ H, straight chain, branched chain or cyclic C_{1-6} alkyl which is unsubstituted or substituted by or substituted by halogen, nitro, $CONH_2$, COOH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, O-C_{2-6} alkynyl, hydroxyl, amino, or COOQ, C_{2-6} alkenyl which is unsubstituted or substituted by or substituted by halogen, nitro, $CONH_2$, COOH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, O-C_{2-6} alkynyl, hydroxyl, amino, or COOQ, C_{2-6} alkynyl which is unsubstituted or substituted by or substituted by halogen, nitro, $CONH_2$, COOH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, O-C_{2-6} alkynyl, hydroxyl, amino, or COOQ, C_{1-6} acyl, or a ~~an~~ hydroxy protecting group;

D_1 and D_2 are each independently ~~selected from~~ N_3, F, or H, wherein D_1 and D_2 are not both H; or

D_1 and D_2 together form ~~can also be joined to be chosen from~~ C_3-cycloalkyl which is unsubstituted or substituted by or substituted by halogen, nitro, $CONH_2$, COOH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, O-C_{2-6} alkynyl, hydroxyl, amino, or COOQ, - $=CH_2$, or - $=CF_2$;

with the proviso that when B is adenine, Z is ORb, D_1 is H, D_2 is H and Rb is H, Ra is not triphosphate or H.

2. A method according to claim 19, ~~1~~ wherein Z is OH.

4. A method according to claim 2, wherein Ra is ~~chosen from~~ H, monophosphate,

diphosphate, or triphosphate.

7. A method according to claim 3, wherein Ra is ~~chosen from~~ H, monophosphate, diphosphate, or triphosphate.

10. A method according to claim 2, wherein B is ~~chosen from~~

adenin-9-yl, guanin-9-yl, inosin-9-yl, 2-amino-purin-9-yl, 2-amino-6-chloro-purin-9-yl, 2-6-diamino-purin-9-yl, thymin-1-yl, cytosin-1-yl, uracil-1-yl, 3-carboxamido-1,2,4-triazol-1-yl, 3-deaza-adenin-9-yl, 3-deaza-guanin-9-yl, 3-deaza-inosin-9-yl, 3-deaza-2-amino-purin-9-yl, 3-deaza-2-amino-6-chloro-purin-9-yl 3-deaza-2-6-diamino-purin-9-yl, 7-deaza-adenin-9-yl, 7-deaza-guanin-9-yl, 7-deaza-inosin-9-yl, 7-deaza-2-amino-purin-9-yl, 7-deaza-2-amino-6-chloro-purin-9-yl, 7-deaza-2-6-diamino-purin-9-yl, 7-deaza-8-aza-adenin-9-yl, 7-deaza-8-aza-guanin-9-yl, 7-deaza-8-aza-inosin-9-yl, 7-deaza-8-aza-2-amino-purin-9-yl, 7-deaza-8-aza-2-amino-6-chloro-purin-9-yl, 7-deaza-8-aza-2-6-diamino-purin-9-yl, 8-aza-adenin-9-yl, 8-aza-guanin-9-yl, 8-aza-inosin-9-yl, 8-aza-2-amino-purin-9-yl, 8-aza-2-amino-6-chloro-purin-9-yl, 8-aza-2-6-diamino-purin-9-yl, 5-aza-thymin-1-yl, 5-aza-cytosin-1-yl, 5-aza-uracil-1-yl, 6-aza-thymin-1-yl, 6-aza-cytosin-1-yl, or 6-aza-uracil-1-yl; ~~each of~~

which in each case is unsubstituted or substituted by at least one of NHR_3, C_{1-6}alkyl, -OC_{1-6}alkyl, Br, Cl, F, I or OH, wherein R_3 is H, C_{1-6}alkyl or C_{1-6}acyl.

11. A method according to claim 3, wherein B is ~~chosen from~~

adenin-9-yl, guanin-9-yl, inosin-9-yl, 2-amino-purin-9-yl, 2-amino-6-chloro-purin-9-yl, 2-6-diamino-purin-9-yl, thymin-1-yl, cytosin-1-yl, uracil-1-yl, 3-carboxamido-1,2,4-triazol-1-yl, 3-deaza-adenin-9-yl, 3-deaza-guanin-9-yl, 3-deaza-inosin-9-yl, 3-deaza-2-amino-purin-9-yl, 3-deaza-2-amino-6-chloro-purin-9-yl 3-deaza-2-6-diamino-purin-9-yl, 7-deaza-adenin-9-yl, 7-deaza-guanin-9-yl, 7-deaza-inosin-9-yl, 7-deaza-2-amino-purin-9-yl, 7-deaza-2-amino-6-chloro-purin-9-yl, 7-deaza-2-6-diamino-purin-9-yl, 7-deaza-8-aza-adenin-9-yl, 7-deaza-8-aza-guanin-9-yl, 7-deaza-8-aza-inosin-9-yl, 7-deaza-8-aza-2-amino-purin-9-yl, 7-deaza-8-aza-2-amino-6-chloro-purin-9-yl, 7-deaza-8-aza-2-6-diamino-purin-9-yl, 8-aza-adenin-9-yl, 8-aza-guanin-9-yl,

8-aza-inosin-9-yl, 8-aza-2-amino-purin-9-yl, 8-aza-2-amino-6-chloro-purin-9-yl, 8-aza-2-6-diamino-purin-9-yl, 5-aza-thymin-1-yl, 5-aza-cytosin-1-yl, 5-aza-uracil-1-yl, 6-aza-thymin-1-yl, 6-aza-cytosin-1-yl, or 6-aza-uracil-1-yl; ~~each of~~

which in each case is unsubstituted or substituted by at least one of NHR_3, C_{1-6}alkyl, -OC_{1-6}alkyl, Br, Cl, F, I or OH, wherein R_3 is H, C_{1-6}alkyl or C_{1-6}acyl.

12. A method according to claim 2, wherein B is ~~chosen from~~ adenin-9-yl, guanin-9-yl, inosin-9-yl, 2-amino-purin-9-yl, 2-amino-6-chloro-purin-9-yl, 2-6-diamino-purin-9-yl, thymin-1-yl, cytosin-1-yl, 5-fluoro-cytosin-1-yl, uracil-1-yl, 5-fluorouracil or 1,2,4-triazole-3-carboxamide base ~~(ribarivin base)~~.

13. A method according to claim 3, wherein B is ~~chosen from~~ adenin-9-yl, guanin-9-yl, inosin-9-yl, 2-amino-purin-9-yl, 2-amino-6-chloro-purin-9-yl, 2-6-diamino-purin-9-yl, thymin-1-yl, cytosin-1-yl, 5-fluoro-cytosin-1-yl, uracil-1-yl, 5-fluorouracil or 1,2,4-triazole-3-carboxamide base ~~(ribarivin base)~~.

14. A method according to claim 1, wherein the compound ~~of formula I~~ is ~~chosen from~~:

~~Compound #1: 3'-deoxycytidine;~~
~~Compound #2: 3'-deoxycytidine-5'triphosphate;~~
~~Compound #3: 5-Fluoro-3'-deoxycytidine;~~
~~Compound #4: 5-Fluoro-3'-deoxycytidine-5'triphosphate;~~
~~Compound #5: 3'-deoxyuridine;~~
~~Compound #6: 3'-deoxyuridine-5'triphosphate;~~
~~Compound #7: 5-Fluoro-3'-deoxyuridine;~~
~~Compound #8: 5-Fluoro-3'-deoxyuridine-5'triphosphate;~~
~~Compound #9: 3'-deoxythymidine;~~
~~Compound #10: 3'-deoxythymidine-5'triphosphate;~~
~~Compound #11: 3'-deoxyguanosine;~~
~~Compound #12: 3'-deoxyguanosine-5'triphosphate;~~

~~Compound #13: 2-N-acetyl-3'-deoxyguanosine;~~

~~Compound #14: 2-N-acetyl-3'-deoxyguanosine-5'triphosphate;~~

~~Compound #15: 5-Methyl-3'-deoxycytidine;~~

~~Compound #16: 5-Methyl-3'-deoxycytidine-5'triphosphate;~~

~~Compound #17: 5-Iodo-3'-deoxycytidine;~~

~~Compound #18: 5-Iodo-3'-deoxycytidine-5'triphosphate;~~

~~Compound #19: 5-Chloro-3'-deoxycytidine;~~

~~Compound #20: 5-Chloro-3'-deoxycytidine-5'triphosphate;~~

~~Compound #21:~~ 3'-fluoro-3'-deoxyguanosine or a pharmaceutically acceptable salt thereof;

~~Compound #22:~~ 3'-fluoro-3'-deoxyguanosine -5'triphosphate or a pharmaceutically acceptable salt thereof;

~~Compound #23:~~ 3'-fluoro 3'-deoxycytidine or a pharmaceutically acceptable salt thereof;

~~Compound #24:~~ 3'-fluoro 3'-deoxycytidine-5'triphosphate or a pharmaceutically acceptable salt thereof;

~~Compound #25: 5-Iodo-3'-deoxycytidine;~~

~~Compound #26: 5-Iodo-3'-deoxycytidine-5'triphosphate;~~

~~Compound #27: 5-Chloro-3'-deoxyuridine;~~

~~Compound #28: 5-Chloro-3'-deoxyuridine-5'triphosphate;~~

~~Compound #29: 5-Bromo-3'-deoxyuridine;~~

~~Compound #30: 5-Bromo-3'-deoxyuridine-5'triphosphate;~~

~~Compound #31: 6-Chloro-3'-deoxyguanosine;~~

~~Compound #32: 6-Chloro-3'-deoxyguanosine-5'triphosphate;~~

~~Compound #33:~~ 3'-spirocyclopropyl-3'-deoxyguanosine or a pharmaceutically acceptable salt thereof;

~~Compound #34:~~ 3'-spirocyclopropyl-3'-deoxyguanosine -5'triphosphate or a pharmaceutically acceptable salt thereof;

~~Compound #35:~~ 3'-difluoro-spirocyclopropyl-3'-deoxyguanosine or a pharmaceutically acceptable salt thereof;

~~Compound #36:~~ 3'-difluoro-spirocyclopropyl-3'-deoxyguanosine -5'triphosphate or a pharmaceutically acceptable salt thereof;

~~Compound #37:~~ 3'-methylene-3'-deoxyguanosine or a pharmaceutically acceptable salt thereof;

~~Compound #38:~~ 3'-methylene-3'-deoxyguanosine -5'triphosphate or a pharmaceutically acceptable salt thereof;

~~Compound #39:~~ 3'-difluromethylene 3'-deoxyguanosine or a pharmaceutically acceptable salt thereof;

~~Compound #40:~~ 3'-difluromethylene 3'-deoxyguanosine -5'triphosphate or a pharmaceutically acceptable salt thereof;

~~Compound #41:~~ 3'-spirocyclopropyl-3'-deoxycytidine or a pharmaceutically acceptable salt thereof;

~~Compound #42:~~ 3'-spirocyclopropyl-3'- deoxycytidine -5'triphosphate or a pharmaceutically acceptable salt thereof;

~~Compound #43:~~ 3'-difluoro-spirocyclopropyl-3'- deoxycytidine or a pharmaceutically acceptable salt thereof;

~~Compound #44:~~ 3'- difluoro-spirocyclopropyl-3'- deoxycytidine -5'triphosphate or a pharmaceutically acceptable salt thereof;

~~Compound #45:~~ 3'-methylene-3'- deoxycytidine or a pharmaceutically acceptable salt thereof;

~~Compound #46:~~ 3'-methylene-3'- deoxycytidine -5'triphosphate or a pharmaceutically acceptable salt thereof;

~~Compound #47:~~ 3'-difluromethylene 3'- deoxycytidine or a pharmaceutically acceptable salt thereof;

~~Compound #48:~~ 3'-difluromethylene 3'- deoxycytidine -5'triphosphate or a pharmaceutically acceptable salt thereof;

~~Compound #49: 9-β-D-xylofuranosyl-guanosine;~~

~~Compound #50: 9-β-D-xylofuranosyl-guanosine -5'triphosphate;~~

~~Compound #51: 9-β-D-xylofuranosyl-cytidine;~~

~~Compound #52: 9-β-D-xylofuranosyl-cytidine -5'triphosphate;~~

~~Compound #53:~~ 3'-azido-3'- deoxycytidine or a pharmaceutically acceptable salt thereof; or

~~Compound #54:~~ 3'-azido-3'- deoxycytidine 5'triphosphate~~;~~ or a pharmaceutically

acceptable salt thereof.

15. A ~~The~~ method according to claim 19, ~~1~~ further comprising administering ~~wherein said compound is used in combination with~~ at least one further therapeutic agent chosen from interferon ~~(IFN)~~, interferon α-2a, interferon α-2b, consensus interferon ~~(CIFN)~~, ribavirin, amantadine, rimantadine, interleukine-12, ursodeoxycholic acid ~~(UDCA)~~, glycyrrhizin and silybum marianum.

16. A ~~The~~ method according to claim 2, further comprising administering ~~wherein said compound is used in combination with~~ at least one further therapeutic agent chosen from interferon ~~(IFN)~~, interferon α-2a, interferon α-2b, consensus interferon ~~(CIFN)~~, ribavirin, amantadine, rimantadine, interleukine-12, ursodeoxycholic acid ~~(UDCA)~~, glycyrrhizin and silybum marianum.

17. A ~~The~~ method according to claim 3, further comprising administering ~~wherein said compound is used in combination with~~ at least one further therapeutic agent chosen from interferon ~~(IFN)~~, interferon α-2a, interferon α-2b, consensus interferon ~~(CIFN)~~, ribavirin, amantadine, rimantadine, interleukine-12, ursodeoxycholic acid ~~(UDCA)~~, glycyrrhizin and silybum marianum.

18. A ~~The~~ method according to claim 14, further comprising administering ~~wherein said compound is used in combination with~~ at least one further therapeutic agent chosen from interferon ~~(IFN)~~, interferon α-2a, interferon α-2b, consensus interferon ~~(CIFN)~~, ribavirin, amantadine, rimantadine, interleukine-12, ursodeoxycholic acid ~~(UDCA)~~, glycyrrhizin and silybum marianum.--